

EMETINE PERIODIDE IN THE TREATMENT OF *S. HAEMATOBIIUM* INFECTIONS AMONGST WEST AFRICAN CHILDREN

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The value of emetine in the treatment of schistosomiasis appears to have been first described by Hutcheson (1913), who recorded five cases of *S. japonicum* infection which improved markedly when treated with this drug. Curiously enough, no notice appears to have been taken of this important discovery until Diamantis (1917) recorded thirty cases of Egyptian bilharziasis successfully treated with emetine. The usual method of administering emetine in the treatment of schistosomiasis is to give from half to one and one-quarter grains of the hydrochloride subcutaneously, intramuscularly, or intravenously, till all symptoms have disappeared and live eggs are no longer passed in the urine; this treatment is then continued for a further variable period, the length of which depends upon the opinion of the individual physician as to what constitutes the minimum amount of emetine necessary to prevent a relapse. Emetine given in this manner appears to have no special advantages over antimony, except in the case of young children, the smallness of whose veins renders the intravenous injection of antimony difficult. Prolonged courses of either drug can readily be given to hospital patients, either at home or in the tropics. It is when the treatment of natives, and more especially the mass treatment of natives, in rural districts is attempted that the great drawback to these drugs becomes evident; both drugs require prolonged courses of injections and the native has a firmly rooted objection to this method of administering medicine, and will not tolerate a long

series of subcutaneous, intramuscular, or intravenous treatments ; even if this dislike be sufficiently overcome to allow of his receiving enough of the drug to relieve his more distressing symptoms, he will at this stage, almost inevitably, depart with his disease uncured and his potential danger to the community unlesened. That this is a very real difficulty is evident from the writings of numerous observers. To quote two instances : Blacklock (1925), writing of mass treatment by injections of antimony, states—‘ My personal opinion is that, situated as we are in Sierra Leone, it would be a waste of time and money to undertake it. I have not yet met a case there who would willingly continue to the end of a long course of treatment. The majority of cases relinquished treatment after about six injections ; if the patient declined to take more and was pressed to do so, it simply meant that urgent affairs quickly called him to a distant village. A mass retreat into the bush would be the chief result of mass treatment here.’ The figures for anti-bilharziasis work in Egypt, as quoted by Khalil (1924), would appear to show that of some fifty thousand cases treated less than half completed the prescribed course of twenty-two and a half grains of antimony ; the first figures regarding attendances given in his report are as follows :—

Rejected as unsuitable for treatment	68
Patients refused treatment	4
Patients treated with colloidal antimony	4
Patients receiving less than 5 grains of tartar emetic	313
" " 5-10	" "	" "	" "	" "	" "	" "	" "	215
" " 10-15	" "	" "	" "	" "	" "	" "	" "	146
" " 15-20	" "	" "	" "	" "	" "	" "	" "	92
" " 20-25	" "	" "	" "	" "	" "	" "	" "	55
" " 25-30	" "	" "	" "	" "	" "	" "	" "	84
" " over 30	" "	" "	" "	" "	" "	" "	" "	19
								Total 1,000

The later figures in this report corroborate the difficulty of persuading natives to complete their courses of treatment.

The West African native, although objecting strongly to all forms of injection, does not appear to extend this prejudice to medicines taken by the mouth and will travel great distances and report daily for long periods in order to obtain drugs of this description. It appears clear, therefore, that any drug capable of curing schistosomiasis by oral administration will prove of very great

value in the tropics, both for the treatment of individual cases, and still more so for the mass treatment of intensely infected areas where the drug can be distributed by a native dispenser, without incurring the risks associated with the giving of subcutaneous injections by an unqualified person. Leiper (1925), commenting on Blacklock's paper, remarks :—' It is on the question of the control of the disease, however, that I especially wished to speak, and I would put in a word for antimony as a prophylactic ; not as it is available at present, but through a simple method of giving antimony by the mouth, which, I hope, further work may reveal. Measures which will involve a combination of antimony by the mouth, with some method of attacking the snail, are those upon which I imagine ultimate success will depend.'

So far as the present writer is aware, no preparation of antimony suitable for the treatment of schistosomiasis by oral administration has as yet appeared on the market ; but the figures which follow appear to suggest that in emetine periodide we have a drug which may prove of great value in the oral treatment of schistosomiasis in the tropics.

EMETINE PERIODIDE.

Emetine periodide was first prepared and described by Martindale (1923). Willmore (1923) treated ninety-one cases of amoebic dysentery with emetine periodide and recorded forty-three (47 per cent.) as presumably cured and forty-eight (53 per cent.) as having relapsed. Gordon (1923) treated sixteen cases of amoebic dysentery with the same drug, ten cases (62 per cent.) relapsed. Willmore refers to emetine periodide in the following terms :—' So far, emetine periodide appears to be by far *the most effective, and, at the same time, the least toxic, of all the emetine preparations which I have tried.* . . . E.P.I. (as emetine periodide may be called for short) has the great advantage of allowing an intensive course of 90 grains to be given in the short period of fifteen days, and, if necessary, this may be repeated after about ten days' interval ; compared with E.B.I., it therefore materially shortens the period of hospitalisation, and thereby affects a distinct economy in hospitals and pensions administration, in spite of its high price.'

EXAMINATION AND CLASSIFICATION OF CASES

An examination of eighty-one children at the 'United Brethren in Christ' Missionary School, Jiama, Nimmi Korro, showed that forty-three of them were suffering from *S. haematobium* infection of the bladder; of these forty-three cases, twenty-eight were severe cases; that is to say, they were passing many live eggs and much blood in every sample of urine examined. These twenty-eight severe cases were divided into two classes of fourteen each, care being taken that the average degree of severity of infection was about equal in the two classes; one of these classes (Class I) received emetine hydrochloride treatment given subcutaneously, the other (Class II) emetine periodide treatment given by the mouth. The ages of the twenty-eight cases varied from six to seventeen years, the average age of the emetine hydrochloride group being eleven years and six months, and that of the emetine periodide group nine years and seven months; the age of each child is given in the tables and it can be seen that the result of the treatment seems to be quite uninfluenced by the age of the child.

The urine of each of the twenty-eight cases was examined microscopically every alternate day during the treatment and for eight days after the completion of the course. During the first three days of treatment, while all the children were still passing large numbers of live eggs and no dead eggs, the deposit from an uncentrifuged specimen of urine was examined; from the third day onwards all urines were centrifuged before being examined. In cases where the actual number of eggs per cover-slip preparation is not shown the sign +++ is used to denote a heavy infection, ++ to denote a moderate infection, and + to denote a scanty infection.

CLASS I. SUBCUTANEOUS INJECTIONS OF EMETINE HYDROCHLORIDE

In Table I is shown the curative effect of emetine hydrochloride treatment on fourteen West African children aged nine to seventeen, who were suffering from severe infections of *S. haematobium*. Cases 1-13 received half a grain of emetine hydrochloride, given subcutaneously, once a day on fifteen consecutive days. Case 14 missed four days' treatment, but only one examination, about the

TABLE I.

Showing the curative effect of subcutaneous injections of emetine hydrochloride on fourteen West African children severely infected with *S. haematobium*.

		Before Treatment	Days after first day of treatment											
			1	3	5	7	9	11	13	15	17	19	21	
Case 1 Male Age 9	Live eggs ...	+++	++	+++	++	+	o	o	o	o	o	o	o	
	Dead eggs	o	o	o	o	+	++	o	2	o	o	o	o	
Case 2 Male Age 9	Live eggs ...	+++	++	+	+	o	o	2	2	o	o	o	o	
	Dead eggs	o	o	o	+	1	o	1	o	1	o	o	o	
Case 3 Male Age 12	Live eggs	+++	+++	+++	+++	+++	++	++	+	+	+	o	o	
	Dead eggs	o	o	o	o	o	++	++	+	++	++	8	4	
Case 4 Male Age 11	Live eggs ...	+++	+++	+++	++	++	1	o	1	1	2	o	o	
	Dead eggs	o	o	o	++	o	1	+	o	o	o	3	+++	
Case 5 Male Age 10	Live eggs ...	+++	++	++	+	+	o	+	o	o	o	o	o	
	Dead eggs	o	o	o	o	+	+	+	1	1	o	o	1	
Case 6 Male Age 14	Live eggs ...	+++	+++	++	++	++	o	o	o	2	1	o	o	
	Dead eggs	o	o	o	o	o	+	o	o	o	2	o	o	
Case 7 Male Age 16	Live eggs ...	+++	+++	+	o	o	1	o	o	o	o	o	o	
	Dead eggs	o	o	o	+	o	o	o	o	o	o	o	o	
Case 8 Male Age 9	Live eggs ...	+++	+++	+++	++	+	o	1	o	o	o	o	o	
	Dead eggs	o	o	o	++	o	+	o	+	o	o	o	o	
Case 9 Male Age 10	Live eggs ...	+++	+++	+++	++	++	+	o	2	o	2	o	o	
	Dead eggs	o	o	o	o	++	+	o	o	1	10	1	1	
Case 10 Male Age 10	Live eggs ...	+++	+++	+++	++	++	o	o	o	o	o	o	o	
	Dead eggs	o	o	o	o	++	1	1	o	o	1	o	o	
Case 11 Male Age 9	Live eggs ...	+++	+++	+++	+++	++	++	o	o	o	o	o	o	
	Dead eggs	o	o	o	o	o	+	o	1	o	1	3	o	
Case 12 Female Age 12	Live eggs ...	+++	+++	+++	+++	+++	++	++	++	++	1	5	o	
	Dead eggs	o	o	o	o	o	++	++	+	++	o	5	2	
Case 13 Female Age 13	Live eggs ...	+++	+++	+++	+	+	o	o	+	o	o	o	o	
	Dead eggs	o	o	o	o	+	+	o	++	o	o	o	1	
Case 14 Male Age 17	Live eggs ...	+++	++	+	++		o	o	o	o	o	o	o	
	Dead eggs	o	o	o	o		1	o	1	o	o	o	o	

middle of the course, and was given four days' extra treatment at the end of the course. Considerable difficulty was experienced in making the children attend for their injections and disciplinary action had to be taken to ensure that each child completed its full course. Several cases of 'emetine nodules' and sore arms resulted from these fifteen days of consecutive injections, while one child, four days after the completion of his treatment, developed some rather alarming signs of heart failure which disappeared after two days' rest in bed.

CLASS II. ORAL ADMINISTRATION OF EMETINE PERIODIDE

In Table II is shown the curative effect of emetine periodide, given by the mouth, on fourteen West African children, aged six to thirteen years, who were suffering from severe infections of *S. haematobium*. Cases 1-10 received one grain of emetine periodide orally three times a day on fifteen consecutive days; cases 11, 12, and 13 received the same treatment but missed one day's treatment about the middle of the course and were given an extra day's treatment at the end of the course. Case 14 left school after completing ten consecutive days of treatment. The emetine periodide was supplied in gelatine capsules, but owing to previous experience of gelatine capsules passing through the gut unchanged the powder was removed from the capsule and given mixed with a little milk. It was previously noted by the writer (Gordon 1923) that this method of administering the drug never produced vomiting and the present series of cases confirmed this observation; amongst a total of six hundred and thirty doses administered, vomiting only occurred once, and as the same child completed its course without any further trouble the vomiting was probably independent of the drug. No unpleasant symptoms, such as those recorded with the use of emetine hydrochloride, followed the taking of emetine periodide by mouth, and it is important to note that no difficulty whatsoever was experienced in getting the children to report for, and take, their medicine.

It will be seen from Table I that all fourteen children treated with emetine hydrochloride subcutaneously had ceased to pass live ova at the end of the eight-day observation period. Table II

TABLE II.

Showing the curative effect of oral administration of emetine periodide on fourteen West African children severely infected with *S. haematobium*.

		Before Treatment	Days after first day of treatment										
			1	3	5	7	9	11	13	15	17	19	21
Case 1 Female Age 7	Live eggs ...	+++	+++	++	+	+	+	+	+	0	0	0	0
	Dead eggs	0	0	0	0	+	+	+	+	20	4	7	2
Case 2 Male Age 9	Live eggs ...	+++	+++	+++	+++	+++	++	++	++	++	++	++	++
	Dead eggs	0	0	0	0	0	0	++	+	+	0	+	+
Case 3 Female Age 12	Live eggs ...	+++	+++	+++	+++	++	+	+	++	++	+	+	0
	Dead eggs	0	0	0	0	0	+	++	+	+	++	++	++
Case 4 Male Age 10	Live eggs ...	+++	++	+++	++	+	0	2	0	0	0	0	0
	Dead eggs	0	0	0	0	0	+	0	0	1	0	0	0
Case 5 Male Age 6	Live eggs ...	+++	+++	++	+++	++	0	0	0	0	0	0	0
	Dead eggs	0	0	0	0	0	1	0	0	0	3	0	0
Case 6 Male Age 8	Live eggs ...	+++	+++	++	+++	+	0	0	5	0	1	0	0
	Dead eggs	0	0	0	0	+	2	4	2	10	0	1	0
Case 7 Male Age 10	Live eggs ...	+++	+++	++	+	+	1	0	0	0	+	+	0
	Dead eggs	0	0	0	0	+	0	2	2	5	+	+	1
Case 8 Male Age 8	Live eggs ...	+++	+++	+++	++	+	0	1	0	0	0	0	0
	Dead eggs	0	0	0	0	0	0	1	0	0	0	3	0
Case 9 Male Age 11	Live eggs ...	+++	+++	++	+++	0	+	+	+	0	0	0	1
	Dead eggs	0	0	0	0	0	0	+	+	2	++	4	+
Case 10 Male Age 11	Live eggs ...	+++	++	+++	++	0	0	0	0	7	2	1	0
	Dead eggs	0	0	0	0	2	+	2	0	11	8	3	0
Case 11 Male Age 8	Live eggs ...	+++	+++	++	++	+	0	0	0	0	0	0	0
	Dead eggs	0	0	0	0	0	0	0	0	1	0	0	0
Case 12 Male Age 8	Live eggs ...	+++	+++	++	+++	++	0	0	+	0	0	0	0
	Dead eggs	0	0	0	0	+	0	0	0	1	0	1	10
Case 13 Male Age 13	Live eggs ...	+++	+++	+++	++	++	+	+	+	2	0	0	0
	Dead eggs	0	0	0	++	++	+	+	+	8	3	1	++
Case 14 Male Age 13	Live eggs ...	+++	++	++	++	+	0						
	Dead eggs	0	0	0	++	++	1						

shows that twelve of the fourteen children, treated with emetine periodide by the mouth, had ceased to pass live ova at the end of the same observation period, while the remaining two cases were passing a mixture of live and dead eggs. The Tables also show that with both forms of treatment the urinary findings of the patients continued to improve for some time after the cessation of treatment, so that it is possible that if the observation period had been longer these two cases might also have become negative. It is, of course, impossible to predict how many of the apparently cured cases will relapse. It was at first proposed to re-examine the children a few months after the completion of their treatment, but as all the cases are living in an intensely infected area, a positive finding under such conditions would be of no value. The absence of all unpleasant symptoms following the oral administration of one grain of emetine periodide three times a day for fifteen consecutive days suggests that a larger dose might possibly have been employed with safety.

CONCLUSIONS

1. The oral administration of emetine periodide clears up the urine of children, intensely infected with *S. haematobium*, just as quickly, and almost with as great certainty, as subcutaneous injections of emetine hydrochloride.
2. Certain ill-effects were noted as the result of subcutaneous injections of emetine hydrochloride, and great difficulty was experienced in making the children report for treatment. No ill-effects followed the oral administration of emetine periodide, and no difficulty whatsoever was experienced in getting the children to attend for, and take, this drug.

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